Preparation of Bilayer ODTs with Superior Interfacial Strength Using GRANFILLER-D

■ INTRODUCTION

In recent years, multilayer tablets have drawn attention as dosage form that enable the production of combination drugs with API stability and precisely controlled dissolution rates, and many studies on such tablets have been reported. However, there are still few reports on the application of multilayer tablets for orally disintegrating tablets (ODTs).

In this article, we report preparation of bilayer ODTs using GRANFILLER-D and direct compression which are less prone to delamination.

■ METHODS

1. Preparation and Evaluation of Bilayer OD Placebo Tablets

Placebo tablets using GRANFILLER-D (GNF) were produced. The tablets were examined their hardness, disintegration time, friability and interfacial strength.

Formulation	GNF	Mg-St	Brilliant Blue FCF
White layer	99.0%	1.0%	0%
Blue layer	98.5%	1.0%	0.5%

Bilayer tablets were also produced applying standard formulation in Japan [Lactose/Corn Starch=7/3], and their performance was compared with that of the bilayer ODTs for the same evaluation items.

Formulation	Lactose/ Corn Starch = 7/3	Mg-St	Brilliant Blue FCF
White layer	99.0%	1.0%	0%
Blue layer	98.5%	1.0%	0.5%

2. Preparation and Evaluation of Bilayer ODTs Containing APIs

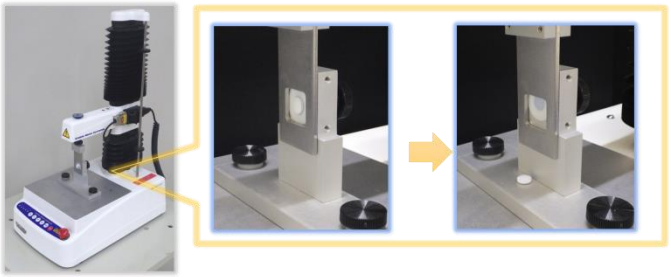
Bilayer ODTs containing APIs were produced. The evaluation items were the same as in the placebo ODTs.

Formulation	GNF	ethenzamide	acetaminophen	LASA	Mg-St	Brilliant Blue FCF
White layer	68.3%	29.7%	0%	1.0%	1.0%	0%
Blue layer	92.5%	0%	5%	1.0%	1.0%	0.5%

Storage stability of bilayer ODTs under unpackaged condition at 40°C/75%RH was also evaluated.

< Measurement of Interfacial Strength >

Interfacial strength was measured by Texture Analyzer (Texture Analyzer TA.XT Plus from EKO INSTRUMENTS CO., LTD.) Pressure was applied to the interface of bilayer tablets to measure the stress (Figure 1).



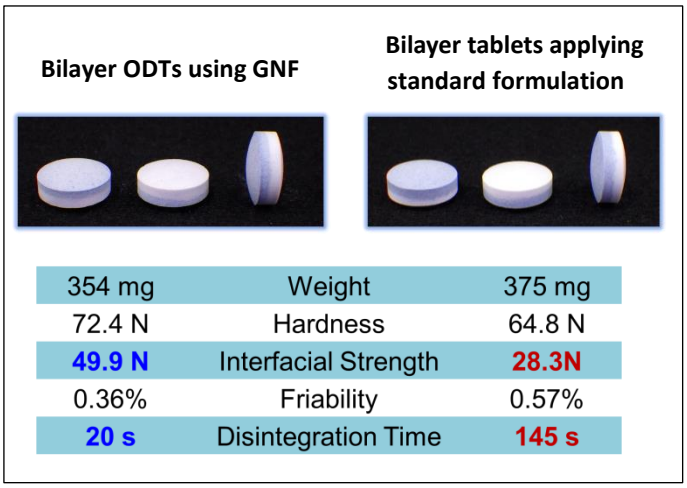
[Figure 1] Measurement of interfacial strength by Texture Analyzer

■ RESULTS

1. Preparation and Evaluation of Bilayer OD Placebo Tablets

Bilayer tablets with a diameter of 10 mm were produced by direct compression using a rotary tableting machine <HT-GS32MS-E/2L>.

Figure 2 shows that the bilayer ODTs prepared using GRANFILLER-D exhibited superior interfacial strength (≥30 N) and still had a shorter disintegration time (≤30 s).



[Figure 2] Comparison of tablet performance

2. Preparation and Evaluation of Bilayer ODTs Containing APIs

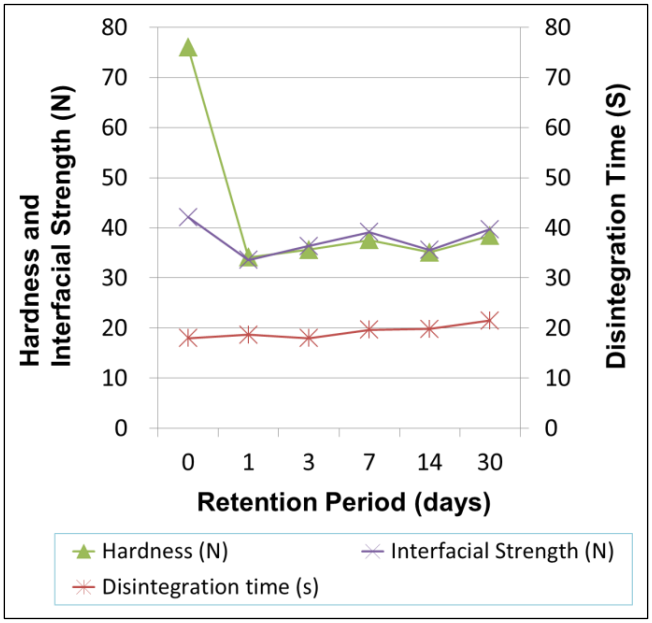
The bilayer ODTs containing APIs also exhibited excellent interfacial strength and a short disintegration time (Table 1).

Tablet hardness decreased approx. 50% by moisture absorption after 1 day, whereas interfacial strength and

disintegration time hardly changed (Figure 3).

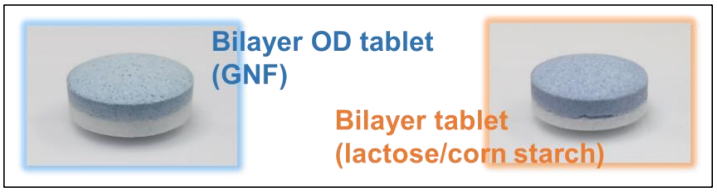
[Table 1] Evaluation of bilayer ODTs containing APIs

Weight	358 mg
Hardness	76.0 N
Interfacial Strength	**42.1 N**
Friability	0.33%
Disintegration Time	**18 s**



[Figure 3] Storage stability under unpackaged condition at 40°C/75%RH

Cracks occurred with bilayer tablet using lactose/corn starch after stability test, but cracks were not observed with bilayer ODTs using GRANFILLER-D (Figure 4).

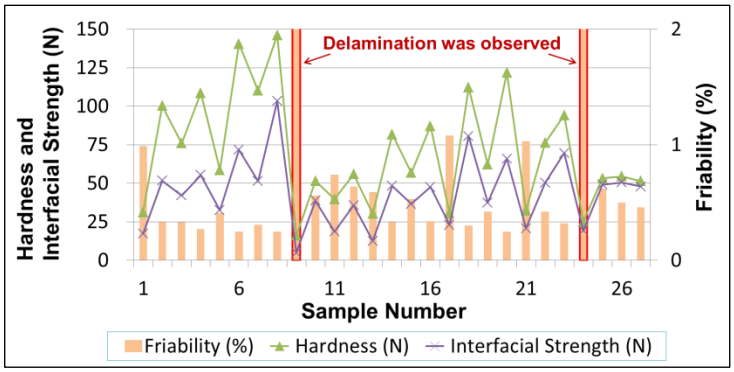


[Figure 4] Tablet pictures after stability test

In order to clarify the relation between the interlayer strength and the delamination, friability tests were conducted with API-containing double-layered ODTs having different interlayer strengths. Delamination was sometimes observed in friability testing, when the interfacial strength was 20 N or less. Therefore, interfacial strength of bilayer tablets is required to be 30N or higher (Figure 5).

■ CONCLUSION

Bilayer placebo ODTs using GRANFILLER-D exhibited both high interfacial strength and short disintegration time. Bilayer ODTs containing APIs also exhibited similar performance, and they showed excellent interfacial strength and short disintegration time even after 1 month stability test. These results suggest GRANFILLER-D may be a suitable for preparation of bilayer ODTs.



[Figure 5] Interfacial strength and friability of bilayer ODTs containing APIs

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